



Serial No.: 09/642,405
Case No.: 20413Y
Page 2

TECH CENTER 1600/2900

OCT 21 2002

RECEIVED

Please substitute the following claims as amended for those previously pending.
A "Version Showing Markings of Pending Claims" is attached hereto which shows the specific amendments to individual claims.

1. (Amended) A synthetic polynucleotide comprising a sequence encoding a codon-optimized human papillomavirus serotype 16 (HPV16) protein, or mutated form thereof which has reduced protein function for viral replication and cellular transformation as compared to wild-type protein, but which maintains immunogenicity, wherein said polynucleotide sequence comprises codons that are optimized for expression in a human host.

6. (Amended) A polynucleotide according to Claim 4 wherein the protein is an HPV16 L1 protein.

9. (Amended) A polynucleotide according to Claim 4 wherein the protein is a mutated form of E1.

10. (Amended) A polynucleotide according to Claim 9 which is an HPV16 E1 protein.

13. (Amended) A polynucleotide according to Claim 4 wherein the protein is a mutated E2 protein.

14. (Amended) A polynucleotide according to Claim 13 which is an HPV16E2 mutated protein.

17. (Amended) A polynucleotide according to Claim 4 wherein the protein is an HPV16E7 protein.

19. (Amended) An adenoviral vaccine vector comprising an adenoviral genome with a deletion in the E1 region, and an insert in the E1 region, wherein the insert comprises an expression cassette comprising:

A) a polynucleotide encoding a codon-optimized HPV16 protein selected from the group consisting of L1, E1, E2, and E7 proteins or mutant forms thereof, wherein said polynucleotide is codon-optimized for expression in a human host cell; and

Claim 1
B) a promoter operably linked to the polynucleotide.

21
21. (Amended) A shuttle plasmid vector comprising a plasmid portion and an adenoviral portion, the adenoviral portion comprising: an adenoviral genome with a deletion in the E1 region, and an insert in the E1 region, wherein the insert comprises an expression cassette comprising:

A) a polynucleotide encoding a codon-optimized HPV16 protein selected from the group consisting of L1, E1, E2, and E7 proteins, wherein said polynucleotide is codon-optimized for expression in a human host cell; and

B) a promoter operably linked to the polynucleotide.

22. (Amended) A vaccine plasmid comprising a plasmid portion and an expression cassette portion, the expression cassette portion comprising:

A) a polynucleotide encoding a codon-optimized HPV16 protein selected from the group consisting of L1, E1, E2, and E7 proteins, wherein said polynucleotide is codon-optimized for expression in a human host cell; and

B) a promoter operably linked to the polynucleotide.

23. (Amended) A plasmid according to Claim 22 wherein the plasmid portion is V1Jns.

24. (Amended) A method for inducing immune responses in a vertebrate which comprises administering to a vertebrate subject between 1 ng and 100 mg of the composition of Claim 1 to the vertebrate.

25. (Amended) A method for inducing immune responses in a vertebrate which comprises administering to a vertebrate subject between 10^{11} - 10^{12} particles of an adenoviral vector carrying the composition of Claim 1 to the vertebrate.

26. (Amended) A method for inducing an immune response against human papillomavirus in a vertebrate, comprising

A) administering to a vertebrate subject a first vector comprising a polynucleotide encoding a codon-optimized HPV16 protein selected from the group consisting

of L1, E1, E2, and E7 proteins, wherein said polynucleotide is codon-optimized for expression in a human host cell;

- 24
25
26
27
- B) allowing a predetermined amount of time to pass; and
 - C) administering to said vertebrate subject a second vector comprising adenoviral vaccine vector comprising an adenoviral genome with a deletion in the E1 region, and an insert in the E1 region, wherein the insert comprises an expression cassette comprises
 - i) a polynucleotide encoding a codon-optimized HPV16 protein selected from the group consisting of L1, E1, E2, and E7 proteins or mutant forms thereof, wherein said polynucleotide is codon-optimized for expression in a human host cell; and
 - ii) a promoter operably linked to the polynucleotide.

28. (Amended) A method for inducing immune responses in a vertebrate comprising

29

A) administering to a vertebrate subject a plasmid vaccine, wherein the plasmid vaccine comprises a plasmid portion and an expression cassette portion, the expression cassette portion comprising:

30
31

i) a polynucleotide encoding a codon-optimized HPV16 protein selected from the group consisting of L1, E1, E2, and E7 proteins, wherein said polynucleotide is codon- optimized for expression in a human host cell; and

ii) a promoter operably linked to the polynucleotide;

B) allowing a predetermined amount of time to pass; and

C) administering to said vertebrate subject an adenoviral vaccine vector comprising an adenoviral genome with a deletion in the E1 region, and an insert in the E1 region, wherein the insert comprises an expression cassette comprising:

i) a polynucleotide encoding a codon-optimized HPV16 protein selected from the group consisting of L1, E1, E2, and E7 proteins or mutant forms thereof, wherein said polynucleotide is codon-optimized for expression in a human host cell; and

ii) a promoter operably linked to the polynucleotide.

30. (Amended) A method of making a codon-optimized HPV16 protein comprising expressing in a human host cell a synthetic polynucleotide encoding a human papillomavirus serotype 16 (HPV16) protein, or mutated form thereof which has reduced protein function for viral replication and cellular transformation as compared to wild-type protein, but